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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,051	10/28/2003	Su Chen	034827-2601	5893
30542 7590 05/27/2009 FOLEY & LARDNER LLP P.O. BOX 80278 SAN DIEGO, CA 92138-0278				
EXAMINER				
MOSS, KERI A				
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1797				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/696,051

**Applicant(s)**

CHEN, SU

**Examiner**

KERI A. MOSS

**Art Unit**

1797

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 September 2008 and 18 February 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4, 6-17 and 30-56 is/are pending in the application.
- 4a) Of the above claim(s) 47-53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-17 and 30-56 is/are rejected.
- 7) ☒ Claim(s) 1-4, 6-8, 30-36 and 46-56 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. Claims 1-4, 6-17, 30-56 are pending.

***Election/Restrictions***

2. Applicant's election without traverse of the species dihydroxy-mono acids in the reply filed on February 18, 2009 is acknowledged. Thus, claims **47-53** are withdrawn from consideration as non-elected claims.
3. Applicant's election with traverse in that same reply is persuasive, therefore, the examiner has withdrawn the election of species requirement for claims 54-56.

Applicant's response to the Election of Species requirement is hereby acknowledged.

4. Applicant's Request for rejoinder of claims 30-45 in the reply filed on September 29, 2008 is hereby acknowledged. Applicant's arguments are persuasive and the Examiner has rejoined Group IV claims 30-45 with elected claims 1-4 and 6-17.

***Response to Amendment***

5. Applicant's arguments with respect to rejoinder of claims 30-45 are convincing. The examiner has rejoined these claims.
6. Applicant's amendments changed the scope of the claims 1-4 and 6-17. Therefore, previous rejection has been withdrawn and replaced with new ground of rejection.
7. Applicant's amendment raises new claim objection as follow.

***Claim Objections***

8. Claims **1-4, 6-8, 30-36 and 46-56** are objected to for incorporation of Table 1 into the claims. Claims 1 and 30 incorporate Table 1 into the claims and dependent claims 2-4, 6-8, 31-36 and 46-56 are properly objected to for the same reasons. Incorporation by reference to a specific figure or table is "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993). MPEP § 2173.05(s).

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims **1-3, 6-8 and 46** are rejected under 35 U.S.C. 102 (b) as being anticipated by Gleispach ET al. (Neuroblastoma Screening: Labeling of HVA and VMA for Stable Isotope Dilution Gas Chromatography-Mass Spectrometry, Supplement to Nutrition, Vol. 11, No. 5, 1995).

Regarding claims 1 and 46, Gleispach et al. teach a method of measuring the amount of an unlabeled organic acid in a sample comprising a) adding to a sample suspected of containing the unlabeled organic acid to be measured an amount of a standard (pages 605-606, Urine Collection and Preparation) comprising one or more oxygen-18 labeled organic acids, wherein at least one of the oxygen-18 labeled organic acids belongs to an organic acid class selected from the group dihydroxy mono-acid (vanillylmandelic acid) and wherein at least one of said oxygen-18 labeled organic acids is structurally similar or identical to the unlabeled organic acid to be measured (homovanillic and vanillylmandelic acid differ by one hydroxyl group); b) processing the sample (p. 605-606); c) measuring the amount of unlabeled organic acid and oxygen-18 organic acid in the processed sample (pgs 605-606; Gas Chromatography-Mass Spectrometry; Results); and d) using the amount of oxygen-18 organic acid measured in step c) to adjust the amount of unlabeled organic acid measured in the processed sample so as to reflect the amount of unlabeled organic acid originally present in the sample (pgs 605-606; Gas Chromatography-Mass Spectrometry; Results).

Regarding claims 2-3, the detection is accomplished by gas-chromatography-mass spectrometry (pgs 605, Gas Chromatography-Mass Spectrometry).

Regarding claim 6, the sample is a urine sample (p. 605).

Regarding claims 7-8, processing results in an enrichment and chemical modification of the unlabeled organic acid in the sample (inherent in the chromatography and mass spectrometry processes).

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gleispach et al as applied to claims 1-2, supra, in view of Shushan et al (US 2002/0019056). See Gleispach et al, supra. Gleispach et al does not expressly teach detecting using liquid chromatography-mass spectrometry. However, gas and liquid chromatography are art recognized equivalents. Shushan et al. demonstrates that LC and GC are art-recognized equivalents ([003]-[0012]). Therefore, it would have been obvious to one of ordinary skill in the art to replace mass spectrometry detection using gas chromatography with liquid chromatography in order to obtain predictable results.

14. Claims 9-15, 17 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gleispach in view of Shaw. See Gleispach et al., supra. Gleispach et

al. does not expressly teach adding to a sample an amount of at least one oxygen-18 labeled organic acid selected from each of hydroxy mono-acid, dihydroxy mono-acid, dicarboxyl organic acid, hydroxyl dicarboxyl acid, tricarboxyl acid, glycine conjugate and keto acid. Shaw teaches that each of these groups hydroxy mono-acid, dihydroxy mono-acid, dicarboxyl organic acid, hydroxyl dicarboxyl acid, tricarboxyl acid, glycine conjugate and keto acid (columns 2-3), when found in abnormal amounts, can be used to demonstrate a diagnosis of autism (abstract). Specifically, Shaw teaches that if the quantities of one or more of the compounds are abnormal, an ultimate diagnosis of autism is likely (abstract). Thus, it would have been obvious for one of ordinary skill in the art to add at least one acid from each of these groups to the sample to gain the advantages of the ability to diagnose autism.

15. Claim **16** is rejected under 35 U.S.C. 103(a) as being unpatentable over Gleispach et al and Shaw as applied to claim 9, supra, in view of Shushan et al (US 2002/0019056). See Gleispach et al in view of Shaw, supra. Neither Gleispach et al. nor Shaw expressly teaches detecting using liquid chromatography-mass spectrometry. However, gas and liquid chromatography are art recognized equivalents. Shushan et al. demonstrates that LC and GC are art-recognized equivalents ([003]-[0012]). Therefore, it would have been obvious to one of ordinary skill in the art to replace mass spectrometry detection using gas chromatography with liquid chromatography in order to obtain predictable results.

16. Claims **30-45** are rejected under 35 U.S.C. 103 (a) as being unpatentable over Gleispach et al, supra, in views of Breakefield et al. (US 5,030,570). See Gleispach et

al, supra. Regarding claim 37, the amount of oxygen-18 organic acid measured in step c) is used to adjust the amount of a structurally similar organic acid measured in the processed sample so as to reflect the amount of the at least one unlabeled organic acid originally present in the sample and the existence of a neuroblastoma is diagnosed by determining whether the unlabeled organic acid originally present in the sample is an abnormal amount (p. 605).

17. While Gleispach et al. teaches a method for diagnosing neuroblastoma, Gleispach et al. does not teach a method for diagnosing the existence of a metabolic defect in an individual. It is well known in the art that abnormally low levels of vanillylmandelic acid demonstrate a metabolic defect in an individual. Breakefield et al. teaches that abnormally low levels of vanillylmandelic acid in urine demonstrate a metabolic defect in an individual (column 10 lines 11-37). Therefore, it would have been obvious to process a urine sample in accordance with the steps disclosed by Gleispach et al. in order to obtain the predictable result of diagnosing a metabolic defect by analyzing whether the amount of unlabeled vanillylmandelic acid detected in the sample is an abnormal amount.

### ***Response to Arguments***

18. Applicant's arguments with respect to claim 1-4 and 6-17 have been considered but are moot in view of the new ground(s) of rejection. Due to the scope change that was caused by newly amended claims, however, upon further consideration, a new



ground(s) of rejection is made in view of Gleispach et al. and also in view of Shaw and Shushan et al, supra.

### ***Conclusion***

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KERI A. MOSS whose telephone number is (571)272-8267. The examiner can normally be reached on 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-1700. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Keri A. Moss/  
Examiner, Art Unit 1797

/Vickie Kim/

Supervisory Patent Examiner, Art Unit 1797